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L1 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2004 ACS on STN

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TI Stable isotope, site-specific mass tagging for protein identification

IN Chen, Xian

PA The Regents of the University of California, USA

SO PCT Int. Appl., 38 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM G01N

CC 9-5 (Biochemical Methods)

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	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002055989	A2	20020718	WO 2002-US538	20020111
	WO 2002055989	A3	20021128		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	US 2002146743	A1	20021010	US 2002-43965	20020111 <--
PRAI	US 2001-261716P	P	20010112		

AB Proteolytic peptide mass mapping as measured by mass spectrometry provides an important method for the identification of proteins, which are usually identified by matching the measured and calculated m/z values of the proteolytic peptides. A unique identification is, however, heavily

dependent upon the mass accuracy and sequence coverage of the fragment ions generated by peptide ionization. The present invention describes a method for increasing the specificity, accuracy and efficiency of the assignments of particular proteolytic peptides and consequent protein identification, by the incorporation of selected amino acid residue(s) enriched with stable isotope(s) into the protein sequence without the need for ultrahigh instrumental accuracy. Selected amino acids(s) are labeled. With  $^{13}\text{C}/^{15}\text{N}/^2\text{H}$  and incorporated into proteins in a sequence-specific manner during cell culturing. Each of these labeled amino acids carries a defined mass change encoded in its monoisotopic distribution pattern. Through their characteristic patterns, the peptides with mass tag(s) can be readily distinguished from other peptides in mass spectra. The present method of identifying unique proteins can also be extended to protein complexes and will significantly increase data search specificity, efficiency and accuracy for protein identifications.

ST stable isotope mass tagging protein

IT Mass spectra

(Delayed-extraction; stable isotope, site-specific mass tagging for protein identification)

IT Mass spectra

(Postsource decay fragment ion; stable isotope, site-specific mass tagging for protein identification)

IT Peptides, analysis

RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)

(UBL1; stable isotope, site-specific mass tagging for protein identification)

IT Proteins

RL: ANT (Analyte); ANST (Analytical study)

(complexes; stable isotope, site-specific mass tagging for protein identification)

IT Mass spectrometers

(electrospray-ionization; stable isotope, site-specific mass tagging for protein identification)

IT Gene

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(expression; stable isotope, site-specific mass tagging for protein identification)

IT Amino acids, uses

RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)

(labeled; stable isotope, site-specific mass tagging for protein identification)

IT Gene

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(lesions; stable isotope, site-specific mass tagging for protein identification)

IT Time-of-flight mass spectrometers

(matrix-assisted laser desorption/ionization; stable isotope, site-specific mass tagging for protein identification)

IT Information systems

(searching; stable isotope, site-specific mass tagging for protein identification)

IT Cell

Composition

Digestion, chemical

Dilution

Escherichia coli

Ionization

Ions

Isotope indicators

Labels

Liquid chromatography

Mass

Mass spectra

Mass spectrometers

Mass spectrometry

Mathematical methods

Mixtures

Protein degradation

Protein sequences

Separation

(stable isotope, site-specific mass tagging for protein identification)

IT Peptides, analysis

Proteins

RL: ANT (Analyte); ANST (Analytical study)

(stable isotope, site-specific mass tagging for protein identification)

IT Proteome

RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)

(stable isotope, site-specific mass tagging for protein identification)

IT Gel electrophoresis

(two-dimensional; stable isotope, site-specific mass tagging for protein identification)

IT 4896-75-7, Glycine-2,2-d2 7782-39-0, Hydrogen-2, uses 14390-96-6,

Nitrogen-15, uses 14762-74-4, Carbon-13, uses 349086-43-7,

L-Methionine-d3

RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)

(stable isotope, site-specific mass tagging for protein identification)

IT 26112-89-0, Isopropylthiogalactoside

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(stable isotope, site-specific mass tagging for protein identification)

IT 9001-92-7, Protease 9002-07-7, Trypsin

RL: CAT (Catalyst use); USES (Uses)

(stable isotope, site-specific mass tagging for protein identification)

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